

What is claimed is:

1. A method of making a mixture of theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin 3,3'-digallate, said method comprising the steps of:
 - contacting green tea leaves with an aqueous buffer to form a reaction mixture;
 - contacting the reaction mixture with oxygen to begin fermentation;
 - fermenting the reaction mixture for a time sufficient to form the mixture of theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin 3,3'-digallate;
 - terminating fermentation; and
 - separating the reaction mixture from the mixture of theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin 3,3' digallate.
2. The method of Claim 1 wherein the separating step further comprises:
 - contacting the reaction mixture with an organic solvent to dissolve the mixture of theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin 3,3' digallate;
 - contacting the solvent with dilute aqueous base;
 - separating the solvent from the base;
 - contacting the solvent with a chromatographic media; and
 - eluting the mixture of theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin 3,3' digallate from the chromatographic media.
3. The method of Claim 2 wherein solids are removed from the reaction mixture prior to contacting with the organic solvent.
4. The method of Claim 2, wherein the medium is silica gel.
5. The method of Claim 1, wherein the ratio of green tea leaves to aqueous buffer is between about 1:0.5 and about 1:20 on a kilogram to liter basis.
6. The method of Claim 1, wherein the aqueous buffer is 0.15 M phosphate buffer at pH 6.4.

7. The method of Claim 1, wherein the reaction mixture is fermented at between about 15 °C and about 80 °C.
8. The method of Claim 7, wherein the reaction mixture is fermented at about 30 °C.
9. The method of Claim 1, wherein the reaction mixture is agitated during fermentation.
10. The method of Claim 9, wherein the reaction mixture is stirred.
11. The method of Claim 1, wherein the time is between about 0.5 hours and about 1.5 hours.
12. The method of Claim 1, wherein the time is about 1 hour.
13. A pharmaceutical composition comprising a mixture of theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof and a pharmaceutically acceptable vehicle.
14. A diet supplement composition comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof and a suitable diet supplement vehicle.
15. A method of treating or preventing hyperlipidemia comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.
16. A method of treating or preventing hyperlipidemia comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 13.

17. An article of manufacture comprising a container, the pharmaceutical composition of Claim 13 and written instructions associated with the container for treating or preventing hyperlipidemia by administering to a patient in need of such treatment a therapeutically effective amount of the pharmaceutical composition.

18. A method of treating or preventing coronary heart disease comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.

19. A method of treating or preventing coronary heart disease comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 13.

20. A method of treating or preventing apoplexy comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.

21. A method of treating or preventing apoplexy comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 13.

22. A method of treating or preventing atherosclerotic cardiovascular diseases comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.

23. A method of treating or preventing atherosclerotic cardiovascular diseases comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 13.

24. A method of treating AIDS comprising administering to a patient in need of such treatment a therapeutically effective amount of a mixture comprising theaflavin,

theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.

25. A method of treating AIDS comprising administering to a patient in need of such treatment a therapeutically effective amount of the pharmaceutical composition of Claim 13.

26. A method of treating or preventing diabetes comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.

27. A method of treating or preventing diabetes comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 13.

28. A method of treating or preventing increased oxidated-low density lipoprotein level in plasma comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.

29. A method of treating or preventing increased oxidated-low density lipoprotein level in plasma comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 13.

30. A method of treating or preventing increased von Willebrand's disease comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.

31. A method of treating or preventing increased von Willebrand's disease comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 13.

32. A method of treating or preventing leukopenia comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.

33. A method of treating or preventing leukopenia comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 13.

34. A method of treating or preventing fatty liver comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.

35. A method of treating or preventing fatty liver comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 13.

36. A method of treating or preventing cerebral infarction comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture of compounds chosen from the group comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.

37. A method of treating or preventing cerebral infarction comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 13.

38. A method of treating or preventing dementia and physical disorder induced by cardio- and cerebral-vascular disease comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate or a pharmaceutically available salt, hydrate or solvate thereof.

39. A method of treating or preventing dementia and physical disorder induced by cardio- and cerebral-vascular disease comprising administering to a patient in need of such

treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 13.

40. A method for making theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate, each as a separate compound, said method comprising the steps of:

contacting tea polyphenols with a aqueous buffer and polyphenol oxidase to form a reaction mixture;

contacting the reaction mixture with oxygen to begin fermentation;

fermenting the reaction mixture for a time sufficient to form a mixture of theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate;

terminating fermentation; and

separating the reaction mixture to provide theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate or theaflavin-3,3'-digallate, each as a separate compound.

41. The method of Claim 40, wherein the separating step further comprises:

contacting the reaction mixture with an organic solvent;

contacting the solvent with dilute aqueous base;

separating the solvent from the base; and

contacting the solvent with a chromatographic media; and

eluting the theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin 3,3' digallate, each as a single compound, from the chromatographic media.

42. The method of Claim 41 wherein solids are removed from the reaction prior to contacting with the organic solvent.

43. The method of Claim 41, wherein the medium is silica gel.

44. The method of Claim 40, wherein theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate or theaflavin-3,3'-digallate are each greater than about 97% pure.

45. The method of Claim 40, wherein the ratio of tea polyphenol to polyphenol oxidase is between about 1:0.1 and about 1:2 on a weight to weight basis.

46. The method of Claim 40, wherein the ratio of tea polyphenol to buffer is between about 1:0.5 and about 1:20 on a kilogram to liter basis.

47. The method of Claim 40, wherein the buffer is 0.15 M phosphate buffer at pH 6.4.

48. The method of Claim 40, wherein the reaction mixture is fermented at between about 15 °C and about 80 °C.

49. The method of Claim 48, wherein the reaction mixture is fermented at about 35 °C.

50. The method of Claim 40, wherein the reaction mixture is agitated during fermentation.

51. The method of Claim 50, wherein the reaction mixture is stirred.

52. The method of Claim 40, wherein the time is between about 0.5 hours and about 1.5 hours.

53. The method of Claim 52, wherein the time is about 40 minutes.

54. A pharmaceutical composition comprising theaflavin, theaflavin-3, theaflavin-3'-gallate or theaflavin-3',3'-digallate or a pharmaceutically available salt, solvate or hydrate thereof and a pharmaceutically acceptable vehicle.

55. A method of treating or preventing hyperlipidemia comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of theaflavin, theaflavin-3, theaflavin-3'-gallate or theaflavin-3',3'-digallate or a pharmaceutically available salt, solvate or hydrate thereof.

56. A method of treating or preventing hyperlipidemia comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 54.

57. A pharmaceutical composition comprising either two or three compounds chosen from the group consisting of theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate, theaflavin-3',3'-digallate and pharmaceutically available salts, solvates or hydrates thereof and a pharmaceutically acceptable vehicle.

58. A method of treating or preventing hyperlipidemia comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a mixture comprising either two or three compounds chosen from the group consisting of theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate, theaflavin-3',3'-digallate and pharmaceutically available salts, solvates or hydrates thereof.

59. A method of treating or preventing hyperlipidemia comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition of Claim 57.

60. A diet supplement composition comprising theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate or theaflavin-3,3'-digallate or a pharmaceutically available salt, solvate or hydrate thereof and a suitable diet supplement vehicle.

61. A diet supplement composition comprising either two or three compounds selected from the group consisting of theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate, theaflavin-3,3'-digallate and pharmaceutically available salts, solvates or hydrates thereof and a suitable diet supplement vehicle.

62. An article of manufacture comprising a container, the pharmaceutical composition of any one of Claims 54 and 57 and written instructions associated with the container for treating or preventing hyperlipidemia by administering to a patient in need of such treatment or prevention a therapeutically effective amount of the pharmaceutical composition.

63. A capsule comprising:
a shell comprising gelatin, water and optionally a plasticizer; and

a fill material comprising a mixture of theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3,3'-digallate;

wherein the shell or the fill material further comprises a radiation blocker and a anti-oxidant.

64. The capsule of Claim 63, wherein the shell is a soft elastic capsule that includes the plasticizer, optionally a colorant and optionally, a radiation blocker.

65. The capsule of Claim 64, wherein the plasticizer is a polyol.

66. The capsule of Claim 65, wherein the plasticizer is a mixture of glycerin and sorbitol.

67. The capsule of Claim 63, wherein the fill material further comprises an anti-oxidant, a pharmaceutically acceptable carrier and optionally, an emulsifier.

68. The capsule of Claim 67, wherein the anti-oxidant is Vitamin E, the pharmaceutically acceptable carrier is soybean oil and the emulsifier is lecithin.

69. The capsule of Claim 67, wherein the fill material further comprises a stiffening agent.

70. The capsule of Claim 67, wherein the stiffening agent is beeswax.

71. The capsule of Claim 1, wherein the shell includes a ultraviolet radiation blocker in an amount sufficient to prevent ultraviolet degradation of the mixture of theaflavins and the fill material includes an anti-oxidant in an amount sufficient to prevent oxidative degradation of the mixture of theaflavins.

72. The capsule of Claim 64, wherein the shell comprises:

between about 25 % and about 45 % gelatin;

between about 1 % and about 30 % plasticizer;

between about 5 % and about 40 % water;

between about 1 % and about 5 % ultraviolet radiation blocker; and

between about 1 % to about 5% colorant.

73. The capsule of Claim 67, wherein the fill material comprises:

between about 1 % and about 20 % mixture of theaflavins;

between about 1 % and about 5 % anti-oxidant;

between about 5 % and about 90 % pharmaceutically acceptable carrier;

between about 1 % and about 20 % emulsifier; and

between about 1 % to about 20 % stiffening agent.

74. The capsule of Claim 63 or Claim 64 further comprising a masticatory substance.